

006953

Reviewed By: Henry Spencer, Ph.D. *5/4/82*  
Section VI, Toxicology Branch (TS-769C)  
Secondary Reviewer: Albin Kocialski, Ph.D. *MBK*  
Section VI, Toxicology Branch (TS-769C) *5/14/82*

# DATA EVALUATION REPORT

Study: Metabolism (Kinetic Study) .

Accession No.: 247156

MRID No.: ~~Not stated~~ 00098321

Test Material: Technical Grade Picloram Lot No. AGR/55434 82.4%  
with 10.9% water, <sup>14</sup>C-ring-labeled picloram.  
S.A. = 10 mCi/mmol (41 mCi/mg).

Study No.: Not provided

Sponsor: Dow Chemical Company

Testing Facility: Dow Chemical Company, Midland, Michigan

Title of Report: Kinetics of <sup>14</sup>C-Labeled Picloram in Male Fischer  
344 Rats by Dow Chemical Toxicology Research Lab.

Authors: Nolan, R.J.; Smith, F.A.; Muller, C.J.; Curl, T.C.

Report Dated: February 4, 1980

Core Classification: Supplementary

## Conclusions:

Three male rats were dosed orally with 1.634 mg/kg,  
9.6 mg/kg; or 184 mg/kg. The test material was given i.v. at  
either 160 or 14 mg/kg.

## Study:

Kinetics of <sup>14</sup>C-Labeled Picloram in Male Fischer 344 Rats  
by Dow Chemical Toxicology Research Lab. dated February 4, 1980.  
Accession No. 247156. Submission dated April 6, 1982.

## Material Tested:

<sup>14</sup>C-ring-labeled (4-amino-3,5,6-trichloropicolinic acid).  
Lot No. 188, GH-14-6-55A and technical grade picloram Lot No. AGR  
155434. Specific activity = 10 mCi/mmol (41 mCi/mg); technical  
grade purity was 82.4% with 10.9% water.

1

Animals:

Fischer 344 rats with 3 male rats/dose level were used (weighing 195 to 250 g).

Methods:

Animals were prepared with right jugular vein cannulae. Food and water were provided ad libitum. Animals were not fasted. Metabolism cages were used with one animal/cage.

Dosages:

i.v. 1. High dose = 160 mg/kg (28 uCi/animal)  
(dose volume = 1.9 mL/kg)

i.v. 2. Low dose = 14 mg/kg (43 uCi/animal)  
(dose volume = 1.9 mL/kg)

Oral 1. 1634 mg/kg = 24 uCi/animal  
(dose volume = 7.3 mL/kg)

Oral 2. 9.6 mg/kg = 20 uCi/animal  
(dose volume = 10.2 mL/kg)

Balance of study (oral) = 184 mg/kg = 9.2 uCi/animal  
(dose volume = 10.2 mL/kg).

Samples:

Feces, urine, and CO<sub>2</sub> were collected and counted for <sup>14</sup>C until 72 hours after sampling.

Blood samples were collected at 5, 10, 15, 20, and 40 minutes as well as 1, 1.5, 2, 3, 4, 6, 8, 12, 18, 24, 30, 36, and 48 hours after the infusions. Urine samples were collected at 3, 6, 9, 12, 18, 24, 36, and 48 hours while feces were collected at 24-hour intervals.

Tissue samples included skin, kidney, liver, G.I. tract and contents, fat and skeletal muscle and remaining carcass.

Samples were either analyzed by scintillation or oxidized directly for <sup>14</sup>C activity.

Results:

Oral balance study with 184 mg <sup>14</sup>C picloram/kg. Three rats gave mean excretion values of 82.28 ± 2.78 percent of the dose in urine, 15.52 ± 2.04 percent of the dose in feces, < 0.006 percent of the dose in CO<sub>2</sub>, and 0.57 ± 0.18 percent in cage washing; for a total of 98.37 ± 1.21 percent recovered after 72 hours.

In either i.v. or oral dosages ranging from 9.6 mg/kg to as high as 1634 mg/kg no less than 84.47 percent on the average of the dose was excreted in 48 hours in the urine; from 2 to approximately 10 percent in the feces. Tissues accounted for from  $0.04 \pm 0.16$  to  $6.48 \pm 3.77$  percent of the dose at 48 hours.

Plasma clearance was 34.3 mL/kg/min with an i.v. dose of 14 mg/g and 14.1 mL/min/kg bwt with an i.v. dose of 160 mg/kg and a plasma half-life was 6.6 minutes.

Comment:

Toxicology Branch questions whether an apparent increase in plasma concentration in Figure 3 page 32 of the report does in fact occur. The extremely small number of animals is hardly sufficient to give a line of "best fit."

This reviewer does not consider this portion of the kinetics profile sufficiently delineated by the paucity of data. The i.v. doses were not carried out far enough to prove or disprove the elevated plasma levels which might have occurred in the oral study at 18 and 30 hours.

Supplementary data.